

### **REMARKS/ARGUMENTS**

In this Amendment, claims 190, 197, 201 and 206 are currently amended; claims 110-112, 114, 154, 157-161, 163, 166-170, 173-178, 180-183, 193-196, 199, 200, 204, 205, 209-211 and 216-229 were previously presented; and claims 1-106, 108, 109, 113, 115-153, 155, 156, 162, 164, 165, 171, 172, 179, 184-189, 191, 192, 198, 202, 203, 207, 208 and 212-215 are canceled without prejudice or disclaimer. It is submitted that no new matter has been added by virtue of the amended claims, which are supported by the claims and the disclosure of the application as originally filed.

Accordingly, the currently pending claims in the application are claims 107, 110-112, 114, 154, 157-161, 163, 166-170, 173-178, 180-183, 190, 193-197, 199-201, 204-206, 209-211 and 216-229.

#### **Support for the Amended Claims**

Support for the amendments to claims 190, 197, 201 and 206 may be found throughout the specification, including, for example, on page 32, Example 3, and Figure 1. *See*, Applicants' disclosure at page 7 continuing to page 8.

#### **Allowable claims**

The Examiner has indicated that claims 220 and 222 are allowed and free of the prior art of record.

#### **The claims fulfill the requirements of 35 U.S.C. §112, first paragraph**

Claims 107-112, 114, 154, 157-161, 163, 166-170, 173-178, 180-183, 185, 216-218 and 223-229 were rejected under 35 U.S.C. §112, first paragraph, as allegedly failing to comply with the written description requirement.

Concerning claims 107, 154, 163, 170, 178, 216 and their respective dependent claims, the Examiner asserts that the limitation "(b) re-plating non-adherent cells from step (a) in a second collagen coated container" is not supported by the instant specification. More specifically, the Examiner alleges that the language in the claims is broader than the

description in the specification because the claims are not limited to a particular range of cell confluency, while the specification describes re-plating in the context of particular adherent cell confluency ranges.

Applicants respectfully disagree with the Examiner's assertion.

As defined by claims 107, 154, 163, 170, 178, 216, step (b) of Applicants' claimed method includes "re-plating non-adherent cells from step (a) in a second collagen coated container." This step is supported by the instant specification at page 29, lines 14-15, which describes that "after approximately one hour, the supernatant [containing non-adherent cells] was removed and re-plated into a fresh collagen-coated container." The specification further discloses that the serial re-plating of supernatant containing non-adherent cells after adherence of the adherent cells in the culture container is repeated, for example, at least three times, until the end population of isolated cells is obtained.

Applicants respectfully point out that the specific adherent cell (e.g., fibroblast) confluency ranges of 15-20% and 30-40% associated with the re-plating of non-adherent cells, are described in the "**Examples**" sections of both priority documents, i.e., U.S. Serial Nos. 60/083,917 and 09/302,896, and of the instant specification. These ranges represent possible confluencies of the adherent cells that may be attained in the cell cultures prior to re-plating the non-adherent cells in another culture container and serve as exemplary teaching in the specifications of the aforementioned applications.

Accordingly, one having skill in the pertinent art would understand that the adherent cell confluency ranges stated in Applicants' specification are disclosed by way of example only. Because cell re-plating procedures were known and practiced in the art as of the effective filing date of the instant application, one having skill in the relevant art would also understand that the adherent cell confluency ranges described in connection with the re-plating technique in Applicants' disclosure provide representative and exemplary guidance to the practitioner. Additionally, it is well established that a claimed invention need not be limited to the teaching of the disclosed examples when the invention is adequately disclosed and described in the specification such that one having skill in the art would know that Applicants had invented the subject matter being claimed.

It is submitted that the instant disclosure teaches that serial platings of the supernatant of the skeletal muscle cell cultures allows the enrichment of small round cells in the culture supernatant after at least 3 platings, e.g., 5-6 platings. (See, e.g., page 29 of the instant specification). As would be understood by the skilled practitioner, with each re-plating step, adherent cells are separated from non-adherent cells in the culture container following adherence of the adherent cells in the container, regardless of differences in the confluency ranges of the adherent cells.

By way of practical, yet nonlimiting, example, Applicants respectfully submit that a suspension of muscle cells from skeletal muscle tissue, as described and claimed by Applicants, may contain differing numbers of adherent cells, e.g., fibroblasts. This is appreciated and accepted by those who are skilled in the art of cell culture and cell plating techniques. As one having skill in the art would also readily understand, depending on the number of adherent cells in a skeletal muscle cell suspension plated in a culture container, the confluency number associated with the adherent cells in the culture may be different, but the non-adherent cells present in the supernatant of the culture may still be serially re-plated in fresh containers following adherence of the adherent cells in order to enrich for small round cells according to Applicants' described method. As known by the skilled practitioner, adherent cells and non-adherent cells in a culture container are visible to the eye using a light microscope.

Indeed, the skilled practitioner in the art would understand when to re-plate non-adherent cells in the cell cultures by following the procedures disclosed and described by Applicants. Applicants' description and parameters of the plating procedure combined with knowledge of those having skill in the art allow a practitioner to understand when adherent cells have adhered in a culture container such that the non-adherent cells in the supernatant may be re-plated in a second container.

Furthermore, it is respectfully submitted that it is not the rule that in every case in which the description of the invention in the specification is narrower than that in the claim there has been a failure to fulfill the written description requirement. Indeed, in some cases, disclosure of a single species may be sufficient written description to support a later claimed

genus, including the species. *Bilstad v. Wakalopulos*, 72 USPQ2d 1785 (Fed. Cir. 2004). In the instant application, Applicants have provided exemplary disclosure of a re-plating technique for non-adherent cells in the context of an exemplary approximate time and representative adherent cell confluency ranges. In the priority documents mentioned above, Applicants provided additional, exemplary adherent cell confluency ranges. Because the re-plating of cells, as well as the separation of adherent and non-adherent cells, are understood in the pertinent art, the disclosure of re-plating non-adherent cells in the context of at least two exemplary species of adherent cell confluency ranges as provided by Applicants is sufficient to fulfill the written description requirement.

Also, in the instant case, it is not unpredictable at what confluencies the skilled artisan may re-plate cells. "The predictability or unpredictability of the science is relevant to deciding how much experimental support is required to adequately describe the scope of the invention." *Capon v. Eshhar*, 76 USPQ2d 1078 (Fed. Cir. 2005). The distinction in the case law is based upon what would be reasonably conveyed to a person skilled in the art at the time of the original disclosure. In the cell plating field, which is a well established, well understood and reasonably predictable field, it is wholly conceivable that describing one or two adherent cell confluency ranges in connection with procedures for re-plating non-adherent cells would convey to a skilled artisan that Applicants have adequately described the step of re-plating cells. See, e.g., *Bilstad v. Wakalopulos*, 72 USPQ2d 1785 (Fed. Cir. 2004). "In the mechanical world – a fairly predictable field – it is wholly conceivable that manipulation in a small number direction may convey to one skilled in the art that Bilstad indeed described manipulation in a 'plurality' of directions."

Because in the instant case, the re-plating of non-adherent cells in culture is not an unpredictable art, Applicants have fulfilled the written description requirement by describing the serial re-plating of non-adherent cells after a muscle cell suspension is plated in a first culture container and the adherent cells have adhered, and by providing at least two different examples of adherent cell confluency ranges associated with the re-plating step. Thus, at the time of filing the instant application, one of skill in the art would conclude that the Applicants were in possession of the instantly claimed method, including step (b) as defined by claims 107, 154, 163, 170, 178, 216 and claims dependent therefrom.

With particular regard to claims 107 and 216, the Examiner has asserted that the limitation “(c) repeating step (b) at least three times” is broader than the previous limitation for step (c) in the claims. The Examiner concluded that one of ordinary skill in the art would not consider this limitation to be supported by the original disclosure.

Applicants respectfully disagree with the Examiner’s assertion regarding claims 107 and 216. Applicants point out that as described in the specification at page 29, lines 19-20, “after approximately 5-6 serial platings, the culture was enriched with small, round cells.” Because the non-adherent cells were re-plated approximately 5-6 times in serial culture, the cells, by necessity, had to have been re-plated at least 3 times to have been re-plated approximately 5-6 times. Accordingly, one of ordinary skill in the art would understand that, at the time of filing the instant application, Applicants were in possession of the invention as defined by claims 107 and 216.

In view of the foregoing, withdrawal of this rejection is respectfully requested.

**The claims fulfill the requirements of 35 U.S.C. §112, second paragraph**

Claims 190, 193-197, 199-201, 204-206 and 209-211 were rejected under 35 U.S.C. §112, second paragraph, as allegedly being indefinite.

The Examiner has asserted that the recited claims are indefinite for reciting “wherein the cells survive over time.” More specifically, the Examiner states that the term “wherein the cells survive over time” is not defined by the claims, that the specification does not provide a standard for ascertaining the requisite degree, and that one of skill in the art would not be reasonably apprised of the scope of the invention.

Applicants do not agree with the Examiner that the phrase “wherein the cells survive over time” is indefinite. Nevertheless, in an effort to progress the prosecution of this application, the relevant claims have been amended to clarify that cells survive “for at least five days”. Support for this amendment may be found throughout the instant specification including, for example, at page 32, Example 3, and Figure 1 (*See*, for example, the description of Figure 1 at page 7 continuing at page 8 of Applicants’ specification).

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Accordingly, in view of the foregoing, it is respectfully requested that the § 112 second paragraph rejection be reconsidered and withdrawn.

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**CONCLUSION**

Applicants respectfully submit that the application is now in condition for allowance. An action progressing this application to issue is courteously urged.

Should any additional fees be deemed to be properly assessable in this application for the timely consideration of this amendment and response, or during the pendency of this application, the Commissioner is hereby authorized to charge any such additional fee(s), or to credit any overpayment, to Deposit Account No. **50-0311**, Reference no. **28682-501-CIP**, Customer Number: **35437**.

Should an extension of time be required for the timely consideration of this Amendment and response, the Commissioner is hereby authorized to grant any such extension of time as may be necessary, and to charge any additional fee(s) owed by Applicants for such extension of time, to the above-mentioned Deposit Account, Reference and Customer Numbers.

If the Examiner believes that it would be helpful to discuss the application to advance the prosecution of the application and claims to allowance, he is respectfully requested to telephone applicants' undersigned representative at (212) 692-6742 and is assured of full cooperation in this effort.

Respectfully submitted,

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